REMARKS

Claims 1, 2, 5, 6, 17, 18, 21-23 and 25-29, the claims under examination at the present time, have been finally rejected as indefinite and as either anticipated by or obvious over Conze et al. These rejections are respectfully traversed for the reasons given below. Applicants are filing herewith a Request for Continued Examination, and reconsideration is respectfully requested.

Claim Amendments

Applicants have made numerous amendments herein to address the Examiner's specific rejections. The Applicants have also amended the withdrawn claims in the same way to allow for rejoinder.

Applicants' amendment and cancellation of certain rejected claims is not to be construed as an admission that the Examiner's rejections were proper. The Applicants continue to believe that the rejected claims are definite, are described in and enabled by the specification, and are neither anticipated by nor obvious in view of the cited references. The rejected claims have been amended and cancelled for the sole purpose of advancing the case to allowance. The Applicants reserve the right to file one or more continuing applications to continue the prosecution of the rejected claims.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 17 and 27-29 have been rejected as indefinite.

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Claim 17 has been amended as indicated to delete the term objected to by the Examiner. Therefore, Applicants submit that the rejection has been overcome.

The Examiner rejected claim 27 for reciting the phrase "numeric complexity." Applicants submit, as recited in the previous response, that support for claim 27 as written can be found at page 6, lines 21-25 of the specification. However, in response to the Examiner's objection to the phrase "numeric complexity," the Applicants have made two amendments: 1) the wording of the text of claim 27 has been changed so as to leave out that phrase and yet still have the claim mean the same; and 2) the limitation of claim 27 has then been incorporated into claim 1 and claim 27 has been cancelled. Therefore, Applicants submit that the rejection has been overcome.

The rejection of claim 28 is not understood as this claim depends on claim 6, not on any claim that recites the phrase "numeric complexity."

Claim 29 has been amended as indicated. Applicants submit that in view of these amendments as explained above, the specific rejections have been overcome.

Rejection Under 35 U.S.C. § 102

Claims 1, 2, 17, 25 and 29 have been rejected as anticipated by Conze et al. Applicants submit that the Examiner seems to be using an unusual interpretation of the teachings of this reference. As stated by co-inventor Dr. Laszlo Takacs in the accompanying Declaration at point no. 8:

> With respect, the teachings of Conze et al. are completely different from the invention and from the

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claims of the pending application. Conze et al. are describing a way to generate a population of monoclonal antibodies against the extracellular domain of a ***known*** protein by overexpressing the ***known*** protein in whole cells (NIH-3T3 cells) and then immunizing mice with the resultant cell line. Thus, the reference does not teach a "complex" analyte mixture as that term is understood by those of skill in the art and as we have described in the patent application. In addition, the "sample" that Conze et al. use as the immunogen is ***NOT*** "***depleted***" of abundant proteins in its own context. In fact, the extracellular region of CDCP1 ***IS*** an "***abundant protein***" in that context. Furthermore, I do not understand the Examiner's comparison of a population of NIH-3T3 cells with plasma. Therefore, I submit that Conze et al. is entirely different from our invention, in purpose, and in detail, and does not teach all of the elements of our invention as it has been claimed. Conze's goal was to produce monoclonal antibodies against a known protein. Our invention aims at discovering multiple markers (which we do not know at the time when we start the experiments).

Thus, Applicants submit that as the cited reference does not teach all of the elements of the indicated claims, the rejection for anticipation has been overcome.

Rejection Under 35 U.S.C. § 103

Claims 1, 2, 5, 6, 17, 18, 21-23 and 25-29 have been rejected as obvious over Conze et al. in view of four additional prior art references - Stroobant, Hoogenboom et al., Andersen et al. and Nagai et al. Applicants submit that none of these references, alone or in combination with Conze et al. in any combination, provides the teachings described above as being lacking in the primary reference. Thus, Applicants submit that the rejections for obviousness have been overcome.

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The Method of the Invention Satisfies a Long Felt Need

Besides being a vehicle to address the prior art rejections, the Applicants have provided the accompanying Declaration of co-inventor Laszlo Takacs to the Examiner to describe a development project carried out since the filing of the instant application. The success of this development project emphasizes the novelty, non-obviousness and value of the claimed method of biomarker development.

Referring to item no. 5, Dr. Takacs states:

> I present below the results of a development project carried out by the licensee company, under the direction of my co-inventors and me, since the filing of the instant patent application. . . .
>
> A challenge in the treatment of lung cancer has been the lack of tools for ***early, pre-symptomatic detection*** of actual ***clinical symptoms*** of lung cancer ***generally present at advanced stages*** of this disease. I describe here the use of the claimed invention as a widely applicable plasma proteome profiling tool, in this case for the discovery of lung cancer specific biomarkers and early stage lung cancer specific biomarker candidates.

The Declaration goes on to describe the details of the experiment, with Dr. Takacs stating in item 5b:

> We identified thirteen lung cancer specific ($p<0.05$) monoclonal antibodies (mABs) and their cognate protein antigens (candidate biomarkers) that ***individually were capable of discriminating between early stage lung cancer patients and their controls***. (emphasis added)

Dr. Takacs then concludes in item no. 6:

> By using an aliquot of the abundant protein-depleted complex analyte, e.g., plasma, directly as the immunogen, as described and claimed in the instant

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application, the method of the invention raises antibodies against the ***natural*** form of the protein antigens present in the complex analyte (i.e., the form of the protein antigens obtained naturally after post-translational processing). ***The method of the invention is extremely efficient at generating high quality biomarker candidates.*** As shown, in this ***one example***, we were able to identify ***thirteen new lung cancer specific monoclonal antibodies and their new cognate protein antigens.*** Previous to our work, only a few plasma biomarkers for lung cancer at any stage had been identified. These previously identified proteins lack sufficient sensitivity and specificity to be useful for any kind of patient screening (Kulpa et al., 2002), and these proteins have no identified utility for early diagnosis in asymptomatic populations (Molina et al., 2003).

Applicants submit that all claims are in condition for allowance. Rejoinder of previously withdrawn claims and allowance of all claims is respectfully requested.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter which would expedite allowance of the present application.

Respectfully submitted,

Laszlo Takacs et al.

Dated: October 14, 2010

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